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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/814,125	04/01/2004	Johan Frostegard	EPCL:010US/10612841	8029

32425 7590 07/16/2009

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ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
07/16/2009	PAPER

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JOHAN FROSTEGARD

Appeal 2009-002066
Application 10/814,125
Technology Center 1600

Decided[1]: July 16, 2009

Before TONI R. SCHEINER, DONALD E. ADAMS, and STEPHEN WALSH, *Administrative Patent Judges*.

ADAMS, *Administrative Patent Judge*.

DECISION ON APPEAL

This appeal under 35 U.S.C. § 134 involves claims 1-14 and 16-26, the only claims pending in this application. We have jurisdiction under 35 U.S.C. § 6(b).

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, begins to run from the decided date shown on this page of the decision. The time period does not run from the Mail Date (paper delivery) or Notification Date (electronic delivery).

STATEMENT OF THE CASE

The claims are directed to a method for diagnosing early cardiovascular disease. Claims 1, 5, and 9 are illustrative:

1. A method for diagnosing early cardiovascular disease comprising (a) contacting a sample of body fluid with phosphocholine and/or a derivative thereof, (b) assessing the presence and/or concentration of antibodies to phosphocholine and/or to said derivative in the sample by measuring antibodies bound to phosphocholine and/or derivative thereof, and (c) diagnosing early cardiovascular disease based on the presence and/or concentration of said antibodies in the sample.

5. The method of claim [1, wherein said early cardiovascular disease comprises atherosclerosis, hypertension or thrombosis and] wherein measuring comprises a radioimmunoassay.

9. The method of claim 1, wherein measuring comprises an enzyme linked immunosorbent assay.

The Examiner relies on the following evidence:

G. Ostermann, et al., *The degradation of platelet-activating factor in serum and its discriminative value in atherosclerotic patients*, 52 Thrombosis Research 529-540 (1988).

Mary A. Smal, et al., *A specific, sensitive radioimmunoassay for platelet-activating factor (PAF)*, 128 J. Immunol. Methods 183-188 (1990).

Jordi Barquinero, et al., *Antibodies against platelet-activating factor in patients with antiphospholipid antibodies,* 3 Lupus 55-58 (1994).

G.I. Muzya, et al., *Reaction of antiphosphatidylcholine antibodies with thrombocyte-activating phospholipid factor and its structural cellular analogues*, 6 Immunologiya 9-16 (1997).

The rejections presented by the Examiner are as follows[2]:

1. Claims 1-3, 6-8, 11-14, 16, 17, 20-23, and 26 stand rejected under 35 U.S.C § 103(a) as unpatentable over the combination of Muzya and Ostermann.

2. Claims 4, 9, 18, and 24 stand rejected under 35 U.S.C § 103(a) as unpatentable over the combination of Muzya, Ostermann, and Barquinero.

3. Claims 5, 10, 19, and 25 stand rejected under 35 U.S.C § 103(a) as unpatentable over the combination of Muzya, Ostermann, and Smal.

We reverse.

PRINCIPLES OF LAW

In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a prima facie case of obviousness based upon the prior art. *In re Fritch*, 972 F.2d 1260, 1265 (Fed. Cir. 1992). On appeal to this Board, Appellants must show that the Examiner has not sustained the required burden. *See Ex parte Yamaguchi*, 88 USPQ2d 1606, 1608 and 1614 (BPAI 2008) (precedential); *Ex parte Fu*, 89 USPQ2d 1115, 1118 and 1123 (BPAI 2008) (precedential); *Ex parte Catan*, 83 USPQ2d 1569, 1570 and 1577 (BPAI 2007) (precedential); *Ex parte Smith*, 83 USPQ2d 1509, 1512-1514, 1519 (BPAI 2007) (precedential).

"The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 416 (2007).

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[2] We recognize the Examiner's objection of claims 21-26 (Ans. 4). This objection is a petitionable matter not subject to review on Appeal. Accordingly, we will not address this objection.

> When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that is was obvious under § 103.

Id. at 421. It is proper to "take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *Id.* at 418. *See also id.* at 421 ("A person of ordinary skill is also a person of ordinary creativity, not an automaton."). "In determining whether obviousness is established by combining the teachings of the prior art, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art." *In re GPAC Inc.*, 57 F.3d 1573, 1581 (Fed. Cir. 1995) (internal quotations omitted).

Muzya and Ostermann:

ISSUE

Does the combination of Muzya and Ostermann make obvious the diagnosis of early cardiovascular disease based on the presence and/or concentration of antibodies to phosphocholine and/or a derivative thereof in a sample of body fluid?

FINDINGS OF FACT

FF 1. Platelet aggregating or activating factor (PAF) "is the chemical 1-O-alkyl-2-acetyl-sn-glycero-3-phosphocholine" and is therefore a derivative of phosphocholine (Reply Br. 3; Spec. ¶ 0025).

FF 2. Muzya teaches that "[p]hospholipid PAF is involved in the regulation of the blood clotting system, the cardio-vascular system and the immune system and is a mediator of inflammation with a range of etiologies, of allergic reactions and many other pathophysiological processes" (Muzya 9: 17-20; *see also* Ostermann 530: 2-5 (PAF "is an extremely potent lipid mediator which is considered to be involved in various inflammatory, respiratory, and cardiovascular disorders" (endnotes omitted)).

FF 3. The aim of Muzya's "study was to investigate the reaction of blood serum containing antiphosphatidylcholine antibodies with PAF and its structural analogues" (Muzya 10: 5-6).

FF 4. Muzya teaches that "[t]o study the way antiphosphatidylcholine (aPC) antibodies bind with phospholipid PAF and its structural analogues, blood serum containing IgM, or IgM and IgG phosphatidylcholine antibodies was taken from patients presenting with obstetric and gynecological pathologies" (Muzya 11: 28-30).

FF 5. Muzya teaches the use of an enzyme immunoassay (EIA) "to study the manner in which aPL antibodies (phospholipid antibodies) bind with PAF and its structural analogues" (Muzya 11: 9-10).

FF 6. To perform the EIA Muzya teaches the adsorption of phospholipids including, *inter alia*, PAF to the wells of polystyrene microplates and the subsequent addition of blood serum samples to the microplate wells (Muzya 11: 10-26).

FF 7. Muzya teaches that the "results of the assay were considered positive if the average OD of the assay sample was greater than the total of the average OD for the negative controls and two average mean square deviations" (Muzya 11: 24-26).

FF 8. Muzya teaches that "[t]he results of this study show that IgM and IgG aPC antibodies in blood serum from patients with obstetric and gynaecological pathologies are capable of binding *in vitro* with PAF and its structural analogues which differ from PAF in the type of bond at the *sn*-1 position: a simple ether bond in the case of PAF and an ester bond in the case of 1-acyl-PAF" (Muzya 14: 3-6).

FF 9. The Examiner finds that Muzya differs from the claimed invention by not "teaching PAF as an indicator for cardiovascular diseases such as atherosclerosis via PAF quantification in serum and plasma" (Ans. 5-6).

FF 10. Ostermann's "study demonstrates a series of strong relationships between serum lipoproteins, degradation of PAF and the manifestation of coronary artery diseases" (Ostermann 536: 13-15).

FF 11. Ostermann teaches that "the degradation of PAF is catalyzed by a specific acetylhydrolase" (Ostermann 536: 20 - 537: 1).

FF 12. Ostermann's "study was undertaken to establish whether serum PAF-acetylhydrolase is useful to discriminate between patients suffering from cardiovascular disease and healthy subjects" (Ostermann 530: 27-30).

FF 13. Muzya teaches that "aPC antibodies can, apparently, bind with PAF in the microenvironment of cells actively producing PAF. It can be suggested that the formation of a compound with an antibody can inhibit the cleavage of PAF by acetylhydrolase" (Muzya 14: 21-23).

FF 14. Ostermann teaches that "[c]onsidering the suggested role of PAF in the development of atherosclerosis . . . it seems quite surprising that the serum capacity to inactivate this highly proinflammatory phospholipid is significantly increased in serum of patients suffering from coronary artery diseases" (Ostermann 536: 16-20).

FF 15. Ostermann teaches that "[a]lthough there is no proof that the relationships between the degradation of PAF in serum and atherosclerosis are causative in nature there are some hints to a possible use of serum PAF-acetylhydrolase as a risk indicator of atherosclerosis" (Ostermann 537: 17-21).

ANALYSIS

Claim 1 is drawn to a method for diagnosing early cardiovascular disease. All other claims on appeal depend directly or indirectly from claim 1. The method of claim 1 comprises the following three steps:

(a) contacting a sample of body fluid with phosphocholine and/or a derivative thereof,

(b) assessing the presence and/or concentration of antibodies to phosphocholine and/or to said derivative in the sample by measuring antibodies bound to phosphocholine and/or derivative thereof, and

(c) diagnosing early cardiovascular disease based on the presence and/or concentration of said antibodies in the sample.

PAF is a phosphocholine derivative (FF 1). Muzya teaches an ELISA wherein PAF is absorbed to wells of a microplate that is subsequently treated with a sample of a body fluid (FF 5-6). Accordingly, Muzya teaches step (a) of Appellants' claimed invention.

Muzya confirms the presence of antibodies to PAF in a sample by measuring antibodies bound to PAF (FF 6-7). Appellants' claims do not require the antibodies to bind exclusively to phosphocholine (*Cf.* App. Br. 4). In this regard, we note that Muzya teaches that IgM and IgG antiphosphatidylcholine (aPC) antibodies are capable of binding PAF, a

phosphocholine derivative within the scope of Appellants' claimed invention (FF 1 and 8). Accordingly, Muzya teaches step (b) of Appellants' claimed invention.

Muzya does not, however, teach that early cardiovascular disease can be diagnosed based on the presence and/or concentration of antibodies to phosphocholine and/or a derivative thereof in a sample of body fluid (FF 9). Ostermann fails to make up for this deficiency.

Ostermann teaches that a relationship exists between coronary artery diseases and *PAF degradation*, which is catalyzed by a specific acetylhydrolase (FF 10 and 11). Therefore, rather than looking at antibodies that bound PAF, Ostermann's study sought to determine if PAF-acetylhydrolase is useful in detecting patients suffering from cardiovascular disease (FF 12). Further, while Muzya suggests that antibodies that bind PAF can inhibit the cleavage of PAF by acetylhydrolase (FF 13), Ostermann reports that it is surprising that a patient's serum capacity to inactivate PAF is significantly increased in patients suffering from coronary artery disease (FF 14). In sum, Ostermann fails to direct a person of ordinary skill in this art to determine the presence and/or concentration of antibodies to phosphocholine and/or a derivative thereof in a sample of body fluid. Instead, Ostermann suggests the "use of serum PAF-acetylhydrolase as a risk indicator of atherosclerosis" (FF 15; *see generally* App. Br. 5).

CONCLUSION OF LAW

The combination of Muzya and Ostermann fails to make obvious the diagnosis of early cardiovascular disease based on the presence and/or

concentration of antibodies to phosphocholine and/or a derivative thereof in a sample of body fluid.

The rejection of claims 1-3, 6-8, 11-14, 16, 17, 20-23, and 26 under 35 U.S.C § 103(a) as unpatentable over the combination of Muzya and Ostermann is reversed.

Muzya, Ostermann, and Barquinero:

ISSUE

Does Barquinero make up for the deficiencies in the combination of Muzya and Ostermann?

FINDINGS OF FACT

FF 16. The Examiner finds that the combination of Muzya and Ostermann differs "from the instant invention in not specifically teaching assay measurements by enzyme-linked immunoassay" (Ans. 7).

FF 17. The Examiner relies on Barquinero to "teach an ELISA assay to measure antibodies against platelet-activating factor (PAF) in patients with autoimmune diseases" (*id.*).

FF 18. The Examiner finds that Barquinero teaches that PAF is "significantly present in patients with syphilis" (*id.*).

ANALYSIS

Each of rejected claims 4, 9, 18, and 24 depend directly or indirectly from claim 1. The combination of Muzya and Ostermann is discussed above. As Appellants explain, "Barquinero is merely cited for teaching ELISA's. . . . Barquinero, whatever it might offer with regard to ELISA

formats, cannot rescue the deficiencies of the other references given that it is directed to examining autoimmune disease, and not CVD" (App. Br. 7). We agree.

CONCLUSION OF LAW

Barquinero fails to make up for the deficiencies in the combination of Muzya and Ostermann.

The rejection of claims 4, 9, 18, and 24 under 35 U.S.C § 103(a) as unpatentable over the combination of Muzya, Ostermann, and Barquinero is reversed.

Muzya, Ostermann, and Smal:

ISSUE

Does Smal make up for the deficiencies in the combination of Muzya and Ostermann?

FINDINGS OF FACT

FF 19. The Examiner finds that the combination of Muzya and Ostermann differs "from the instant invention in not specifically teaching assay measurements by radioimmunoassay" (Ans. 8).

FF 20. The Examiner finds that Smal teaches a "method to evaluate PAF in a specific and sensitive radioimmunoassay [(RIA)]" (*id.*).

FF 21. The Examiner finds that Smal teaches that "RIA was at least as good as the platelet-based assay for PAF but the RIA was simpler to perform, had higher capacity and did not have the draw backs of the inherent variability associated with the bioassay" (*id.*).

ANALYSIS

Each of rejected claims 5, 10, 19, and 25 depend directly or indirectly from claim 1. The combination of Muzya and Ostermann is discussed above. The Examiner fails to establish that Smal makes up for the deficiencies in the combination of Muzya and Ostermann by making obvious the diagnosis of early cardiovascular disease based on the presence and/or concentration of antibodies to phosphocholine and/or a derivative thereof in a sample of body fluid.

CONCLUSION OF LAW

Smal fails to make up for the deficiencies in the combination of Muzya and Ostermann.

The rejection of claims 5, 10, 19, and 25 under 35 U.S.C § 103(a) as unpatentable over the combination of Muzya, Ostermann, and Smal is reversed.

REVERSED

Ssc:

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